The Use of Preserved Human Dura for Closure of Abdominal Wall and Diaphragmatic Defects

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The surgical management of large body wall defects presents special challenges. The prosthetic materials employed for these defects, although readily available, have the disadvantage of susceptibility to infection. Autologous tissue is frequently not available in sufficient quantity. The long-term functional and histologic results of the use of preserved human dura for closure of abdominal wall and diaphragmatic defects have been evaluated. Dural patches were sutured into abdominal wall and diaphragmatic defects of six dogs, using interrupted sutures of Dexon® and Prolene®. The animals were killed eight, 16 and 24 weeks after patch placement. The strength of the material was tested with a pneumoperitoneum prior to death and in all animals it appeared firmly incorporated into the host tissue. Histologically there was a mononuclear inflammatory response seen at eight weeks, with resolution by 24 weeks. Ingrowth of surrounding collagen and muscular tissue produced a firm union between the homologous material and the host tissue. The results of this study indicate that preserved human dura is an excellent material for closure of body wall defects. It appears to be well tolerated by host tissue and maintains its strength over prolonged periods of time.

SURGICAL REPAIR OF LARGE abdominal wall defects frequently presents a significant challenge. As testimony to the difficulty in managing these lesions, a profusion of techniques and materials have been suggested for use in these situations. The various prosthetic materials which have been used possess the advantage of ready availability, but the disadvantage of acting as a residual "foreign body," susceptible to subsequent infection. The use of autologous tissue has also been suggested, but presents the disadvantages of requiring a secondary incision and relatively limited availability. Preserved homologous tissue would appear to be an ideal material for bridging these defects. The present report details our experimental results of the use of preserved human dura for the closure of abdominal wall and diaphragmatic defects.

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Materials and Methods

For the purposes of these experiments, dura fixed and sterilized in betapropiolactone was employed. This dura was obtained at autopsy examination in an unsterile manner, trimmed and placed in a 1% solution of buffered betapropiolactone. After a three hour fixation time the dura was transferred to a buffered saline–plasma solution in which it was stored. Handled in this manner, this material is safely stored for prolonged periods of time, and may be obtained in pieces measuring as large as 10 × 15 cm. Microbiologic evaluation of this dural material has previously revealed it to remain sterile for prolonged periods (Department of Neurosurgery, University of Florida, unpublished material). Immediately prior to its insertion, the preserved dura was washed thoroughly in two L of sterile saline solution, in order to remove all traces of betapropiolactone and buffer solution prior to implantation.

Six mongrel female dogs weighing between 15 and 20 kg were used in these experiments. Under general anesthesia, with controlled ventilation, the entire anterior abdomen was shaved and cleansed with Betadine solution. A supraumbilical midline incision of 6 cm in length was made and the abdominal cavity entered. The left lobe of the liver was reflected medially and a full-thickness defect, measuring 3 cm in diameter, was created in the muscular portion of the left hemidiaphragm. A 3 cm patch of preserved human dura was sutured to this defect with interrupted sutures. One-half of the circumference of the patch was secured with interrupted 4-0 Prolene* sutures while the other half was secured with interrupted 4-0 Dexon.† A full-thickness midline abdominal defect measuring 4 × 5 cm was then created, and a similar sized dural patch was su-

* Ethicon, Inc., Somerville, NJ 08876.

† Davis & Geck, Pearl River, NY 19065.

0003-4932/81/0500/0606 $00.80

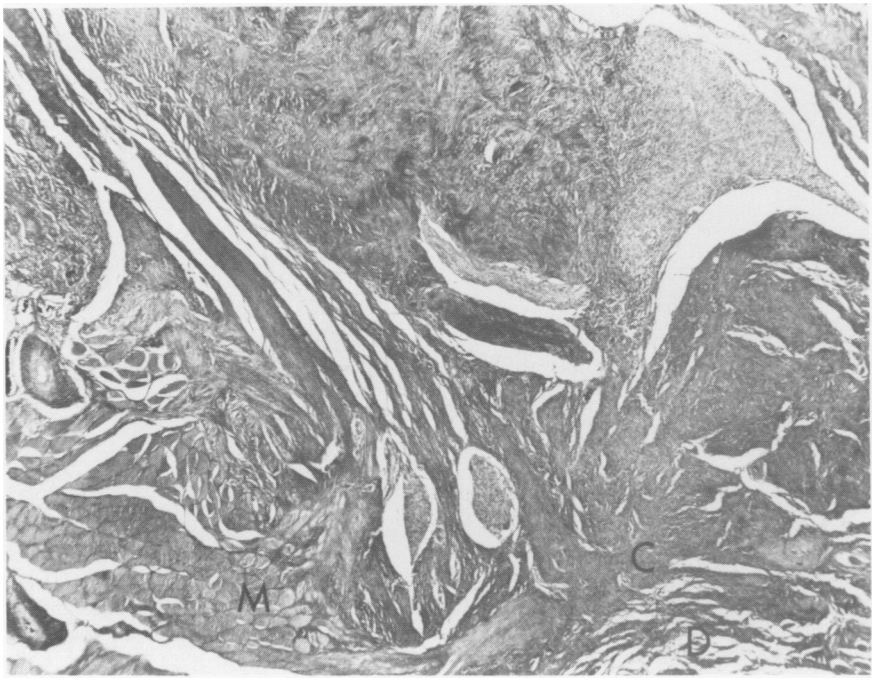

FIG. 1. Photomicrograph of the interface between the abdominal wall musculature (M) and the dural graft (D). In this specimen, obtained from the Prolene side of a graft implanted for eight weeks, there is considerable reactive tissue at the interface. At this stage there is early ingrowth of collagenous tissue (C) into the perimeter of the graft (original magnification ×26).

tured to this defect with interrupted 3-0 Prolene and Dexon sutures. The subcutaneous tissue was closed over this patch with interrupted 4-0 Dexon and the skin was closed with a subcuticular suture of 5-0 Dexon. Each dog received a single, intramuscular injection of procaine penicillin (300,000 units) at the completion of the procedure. The animals were housed in individual cages and allowed an *ad libitum* diet of standard dog chow. Animals were killed in pairs at eight, 16 and 24 weeks following the initial operation.

At the time the animals were killed they were anesthetized with an intramuscular injection of ketamine hydrochloride (1 mg/kg). An 18-gauge needle was passed into the peritoneal cavity through the right lower quadrant and a pneumoperitoneum created. Air was injected to achieve a measured intra-abdominal pressure of 60–80 cm of water. The surgical incision was then inspected and the skin and subcutaneous tissue opened to expose the dural graft and surrounding abdominal wall musculature. This tissue was removed en bloc and fixed in buffered formalin for later microscopic evaluation. A left thoracotomy incision was made to visualize the left diaphragmatic dural patch from the pleural as well as peritoneal side. This tissue was also removed en bloc with a surrounding rim of diaphragmatic musculature and fixed in buffered formalin. The animals were then killed with intravenous pentobarbitol solution. Microscopic sections of the diaphragmatic and abdominal wall dural patches were stained with hematoxylin and eosin as well as Masson stains for histologic evaluation.

Results

All animals tolerated the operative procedure well, and none had evidence of wound infection. When the animals were killed, the abdominal wall and diaphragmatic dural patches appeared to be secure, and in no animal could they be disrupted with the pneumoperitoneum. On the abdominal patch there were occasional loose adhesions between the peritoneal side of the dura and the greater omentum, but there were no adhesions to the underlying bowel. On the diaphragmatic patch, no adhesions to the lung were noted, but most animals had loose adhesions to the left lobe of the liver. There was no evidence of fragmentation of the dural material in these positions, and the Dexon and Prolene closures appeared to be equally secure. By 24 weeks following insertion, both the abdominal wall and diaphragmatic dural patches appeared to have contracted by approximately 25% of their original diameter.

The animals killed at eight weeks following insertion of the dural patch showed microscopic evidence of reactive tissue at the interface between dura and host tissue. This process appeared to be more intense on the side sutured with Prolene, as compared with the Dexon side. At this time there was evidence of a mononuclear-cell infiltrate throughout the dural patch, most prominent at its periphery. In addition, there was early vascularization of the perimeter of the dural material (Fig. 1). The collagenous architecture of the dura itself appeared unchanged.

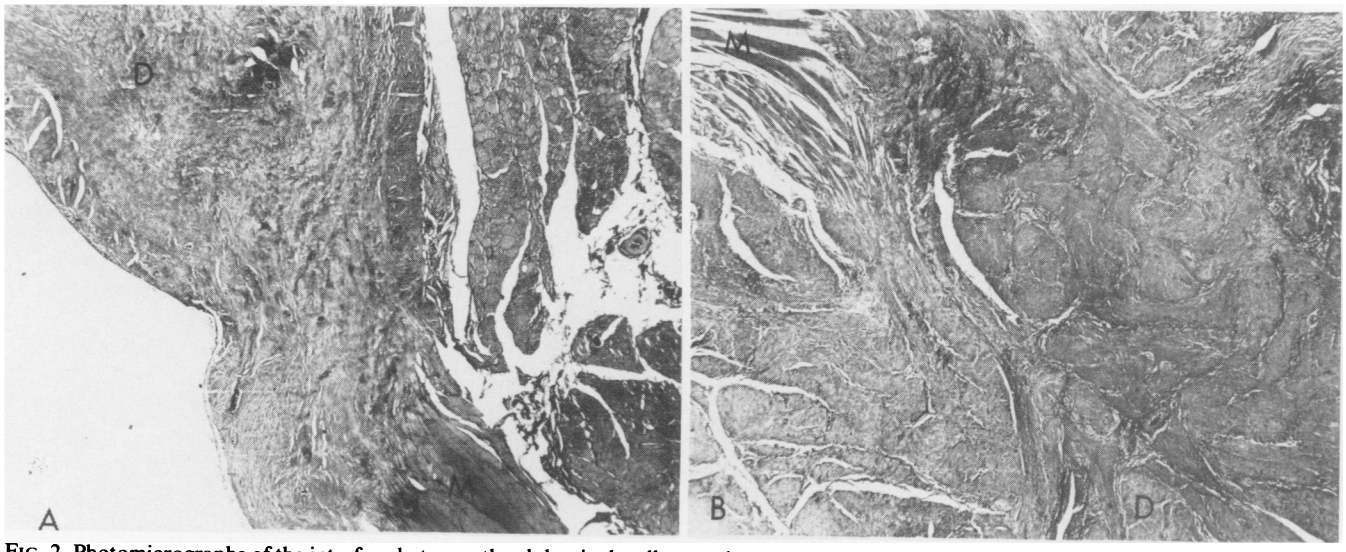

FIG. 2. Photomicrographs of the interface between the abdominal wall musculature (M) and the dural graft (D) of a specimen obtained 16 weeks following implantation. A. On the Dexon side of the graft there is minimal residual inflammatory reaction and considerable infiltration of the periphery of the graft with collagenous tissue. B. On the Prolene side of the graft, the inflammatory reaction persists as collagen grows into the perimeter of the dura (original magnification ×26).

By 16 weeks following patch insertion, the reaction within the dura appeared less intense. In place of the mononuclear-cell infiltrate, there was evidence of muscular and collagenous ingrowth into the dural tissue from the perimeter, and considerably more vascularization of this heterologous tissue. There continued to be a more inflammatory reaction noted on the Prolene side of the dura. In both the abdominal and diaphragmatic patches there appeared to be a neoperitoneum developing by 16 weeks (Fig. 2). By 24 weeks following insertion there was minimal residual inflammatory response. The dura was well incorporated at the periphery by ingrowth of both collagen and muscular tissue, although in neither animal did this ingrowth extend completely across the dural graft (Fig. 3). The collagenous architecture of the dural graft appeared to be well preserved and there was no evidence of ossification in either of the grafts removed at 24 weeks after insertion.

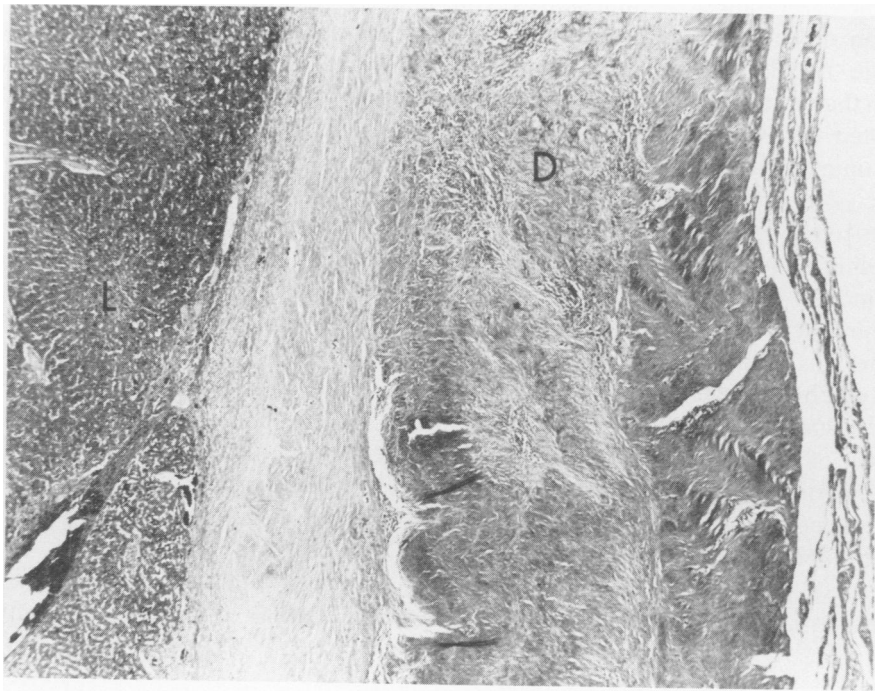

FIG. 3. Photomicrograph of the mid portion of a dural graft implanted for 24 weeks in the diaphragmatic position. The overlapping collagenous architecture of the dura has been maintained and there is minimal residual inflammatory reaction. Collagenous and muscular ingrowth from the host tissue is evident within the mid portion of the dural graft. The interface between the liver (L) and dura (D) is illustrated (original magnification ×33).

Discussion

The ideal abdominal wall and diaphragmatic substitute should have several properties: 1) it should be well tolerated by the host tissue; 2) it should maintain its strength over a prolonged period of time; 3) it should ultimately be incorporated into the host tissue or replaced by it; 4) it should not adhere to or damage the underlying viscera; 5) it should be resistant to infection; and 6) it should be readily available in appropriate sizes. Few of the materials previously employed to close such defects possess all of these properties. The synthetic materials commonly employed, Dacron‡ and Marlex,§ have the advantage of maintaining their strength and being readily available, but persist in the body as a foreign tissue, and are susceptible to the development of infection. Marlex has the additional disadvantage of being relatively stiff and occasionally causing injury to the underlying abdominal viscera, especially in small children.[1] The autologous tissues suggested, principally fascia lata, have the distinct disadvantages of requiring a separate operative incision and of relatively limited availability.

Preserved human dura has been employed for many years for replacement of various body tissues. The use of this material was first suggested in 1955 when investigators at the Naval Medical Research Institute initiated studies directed toward finding a tissue substitute that would be biologically acceptable and could be successfully preserved.[2] Campbell, in 1958, reported clinical results with the use of frozen and lyophilized human dura as a homologous dural substitute.[3] These authors concluded that the collagen within the homologous dura did not survive, but rather served as a lattice for the host connective tissue so that the graft was eventually replaced by the patient's own tissues. These observations have subsequently been corroborated by several authors.[4,5] Maurer, in 1974, fashioned arterial grafts from lyophilized human dura, but found an unacceptably high thrombosis rate in these experiments.[6] Zarbini, in 1975, reported a large experience with cardiac valves fashioned from glycerol-preserved human dura.[7] Under these stresses, the leaflets fashioned for these valves tended to degenerate over time and focci of microcalcification were noted. In many of these studies it has been noted that the implanted dura appeared resistant to local infection, although this property has never been evaluated systematically.

Several authors have reported, in anectodal fashion, the successful use of preserved human dura to repair defects of the chest wall, abdominal wall, and diaphragm.[8,9] Willital recently reported his clinical experience with the use of preserved human dura for the closure of abdominal wall defects in children.[10] Between 1973 and 1979, this author employed this material in 22 patients with excellent results. The mortality rate in children with these complicated defects was comparable to that seen with other methods of management and secure abdominal wall closure was accomplished expeditiously. There appeared to be no tendency for this material to fragment and no ventral hernias were observed in these patients.

The current experiments confirm an excellent acceptability of preserved human dura. Over the six month course of follow-up of these animals, there was no tendency for disruption of this material and no hernias developed, even with the introduction of excessive intra-abdominal pressures. Although the resistance of this material to infection was not systematically evaluated in this study, the absence of wound infection is notable. This material seemed to be extremely well tolerated by the host tissue and formed only minimal adhesions to the underlying viscera. When this material is properly washed in saline, it is pliable and easy to handle. It holds sutures well and does not tend to tear. The histologic evaluation of this material in these studies tends to confirm the occasional clinical biopsy results reported previously. There appears to be an early inflammatory infiltrate along the perimeter of the dura, with subsequent ingrowth of collagen and muscular tissue along with capillaries. The development of a neoperitoneum over the undersurface of this material appeared to minimize the adhesions to underlying viscera. Although the dura was never completely replaced by host tissue in the time interval evaluated in these experiments, it was securely incorporated into the surrounding tissue and showed no evidence of fragmentation. Likewise, there was no evidence of microcalcification in the preserved dura followed for this period of time.

Numerous methods have been suggested for sterilization and preservation of human dura. Whether or not this material is obtained in sterile manner, it must be preserved in a fashion so as not to disturb the overlapping collagenous architecture, which accounts for much of its strength. If the dura is obtained in a sterile fashion, preservation can be achieved with storage in glycerol solution[7] or lyophilization.[3] If the dura is obtained in an unsterile manner, sterilization and preservation has been suggested by emersion in ethylene oxide with subsequent lyophilization[4] or emersion in betapropiolactone. At the time these studies were performed, most investigators recommended sterilizing and fixing this material with betapropiolactone and storing it in a buffered solution. More recently, there has been the suggestion of carcinogenicity of betapropiolactone when applied in large doses to experi-

‡ U.S. Catheter and Instrument Corporation, Billerica, MA 01821.

§ Davol, Inc., Cranston, RI 02920.

mental animals.[11] Because of concern with these findings, most clinicians have discontinued the use of betapropiolactone and have now turned to the use of commercially available lyophilized human dura. Although there have been no long-term experimental studies with dura preserved in this fashion, the clinical evaluations would suggest similar excellent durability.[3]

Preserved human dura offers a very attractive material for the closure of large abdominal wall or diaphragmatic defects. An essentially acellular collagenous tissue, it is low in antigenicity and appears to be well tolerated by the host. It is rapidly bonded to the adjacent tissue by ingrowth of fibroblasts and muscle. The preserved dura maintains its strength well and appears to be resistant to subsequent infection. This material is readily available in pieces as large as 10 × 15 cm and larger pieces may be fabricated by suturing two smaller sheets together. Further studies are indicated to evaluate the long-term fate of lyophilized dura and to evaluate its resistance to infection.

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Discussion

Dr. Duane G. Hutson (Miami, Florida): We were stimulated several years ago to use this material for the repair of abdominal wall defects by Dr. Ted Malinin. I think it's fair to say that most of us at the University now prefer this material for the very reasons that have been so clearly shown, particularly in situations where we feel there might be a possibility of infection.

The difference in our technique and those presented by the authors is that we are using freeze-dried dura, (slide) and this is just an example of one of the freeze-driers that are presently in use.

(slide) This is work which was done by Dr. Hubert Rosomoff, in 1958, relative to allografts of dura used in intracranial operations; and you can see that, after four weeks, he was able to remove this dura implant since no adhesions developed between the dura and the underlying brain tissue. Presently, this appears to be the most common use of this material.

(slide) We have been interested in other applications of this as well, and this is some work that was done by Dr. Swenson, whom I'm sure most of this audience know. When he was in Miami, he did some work in dogs on partial replacement of the bladder, and I am told that these dogs functioned quite well, with no evidence of leakage, and so on.

(slide) Because of the recent increase in trauma in Miami, we have become interested in attempting to replace major vessels with this material, and, indeed, it appears that this is feasible. The reason for our interest, of course, relates to situations where there is concomitant injury of the colon or other sources of contamination. This is the aorta of an animal some four weeks after a dural graft was used to replace the distal aorta.

(slide) We also tried this in the venous system, and, as you might guess, it failed. These grafts can be fabricated, or designed, in any way that you choose. (slide) This is an attempt at an aortobifemoral graft. It has the obvious advantage that you don't have to preclot it. It has the obvious disadvantage that it takes about three days to sew it all together.

(slide) This is a dural graft that was placed in a defect in the peritoneum; and when we opened this animal at approximately four weeks, all of these little dots here represented attachment of the bowel to the dura. The adhesions were not very dense, and were easy to remove, so I think that our study pretty well agrees with what has been presented, although we did find that there was bowel adherent to this tissue.

(slide) This is just granulation tissue that has developed, and at four weeks we didn't see much ingrowth of fibrous tissue into the graft, although we suspected that this would ultimately occur.

(slide) One of the questions that we're always asked is: why not use fascia lata? First of all, dura from a tissue-banking point of view is readily available whereas fascia lata is not. Second, it seems to be much stronger than fascia lata.

I have two specific questions: first, would you comment on the difference in adhesions noted in the two studies and, second, on your preference for dura over fascia lata.

Dr. Emmett Dupree (Jacksonville, Florida): It was my privilege and opportunity to work for two years in the U.S. Navy Tissue Bank at the Naval Research Institute in Bethesda during 1968 and '69, and during this period I and others reviewed and evaluated the use of various human tissues for transplantation. We also carried out some studies on the effects of freeze drying and various types of sterilization used to prepare and preserve tissues prior to transplantation.

Among these materials that were studied was human dura, which at that time was being used in large quantities by neurosurgeons to repair severe head injuries in Vietnam.

(slide) The first slide outlines the practical characteristics of an ideal dural graft, that of workable consistency, ready availability—it's low in cost, and it has a potential for sterilization.